MEN AND BOOKS

Claude Bernard, 1813 - 1878:

The Founder of Modern Medicine

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THE proud Empire of the French under Napoleon I was approaching its unhappy ending when Claude Bernard was born, just 150 years ago, on July 12, 1813. He was born in a farmhouse overlooking the village of Saint-Julien, canton de Villefranche (Rhône), and lived through the troubled times of the restoration of the elder branch of the Bourbons, Louis XVIII and Charles X; the reign of timid Louis Philippe; the 2nd Empire of Napoleon III; the Commune and the establishment of the Third Republic; to be honoured by a state funeral at his death in 1878, the first occasion when a nation wept at the bier of a scientist.

His father, Pierre Bernard, was a prosperous proprietor of two vineyards, but entering the wine business at the fall of the First Empire was a disastrous commercial adventure in which he lost his property and then became the village schoolmaster. State supervision of education hardly existed before 1833 and his pupils attended at his own house for elementary instruction. Pierre Bernard died in 1847, just as his son was commencing to make his mark.

Of his affection for his mother, who preferred to live in the country with her daughter and grandchildren, there is ample testimony. She lived to 1867, 78 years of age, the humble but proud mother of a son whose fame had become world-wide. Claude Bernard meantime had reacquired the family property and used it for recreation, but also, as proprietor, to grow the grapes and make the *vin du pays,* that beauteous red wine of so many merits of the ancient province of Beaujolais. Whenever an opportunity arose, he visited his mother, rested, meditated, dreamed and planned, and wrote of his investigations. During some periods of prolonged illness he preferred the country home to life in the city and found there healing and restoration, or, as we would say today, "rehabilitation" more than merely physical. It was a pleasant land in which the boy grew up, rolling country, covered with the vineyards interspersed with wooded valleys and brooks running down the hillsides to join the river Saône, and, far away to the east, the majestic summits of the snow-covered Alps. A small cottage on the hill, Chatenay, sheltered by a clump of trees on one side and an orchard on the other, was home to him and to a younger sister. Comparatively little is known of his boyhood. Country districts in those days were more remote from urban civilization than at present. The boy was 14 years of age before the first railway was started in France, and doubtless the pulling and hauling, the tumult of the restoration of the Bourbons were little felt apart from the great cities. He was introduced to Latin by the parish priest, and attended the Jesuit College of Villefranche, where he was taught Latin, a little Greek, French, arithmetic and geometry, but neither science, history nor geography, and no modern foreign languages. He seems to have been an indifferent student, serious and introspective, dreamy and silent, and failed to impress his instructors or fellow students with his future potentialities.

At 18, family finances failing, he became employed as a pharmacist's apprentice in Lyon where he rather signally failed to please his patron with his talent for pharmacy, though receiving a testimonial certifying to his honour and fidelity and to be of "whatsoever use to him, it may". There followed a period of unemployment during which he completed a play, "Arthur de Bretagne" which he had commenced while in M. Millet's employ and which was the probable cause of the latter's dissatisfaction.

With a small sum in his pocket and his completed manuscript, Claude Bernard set out for Paris late in 1834, where an introduction to the Professor of Literature, M. Saint-Marc Gérardin, had been arranged. The play was not without merits but the professor, concerned for his future, advised the young man to adopt a profession for his livelihood. The drama was published nine years after Bernard's death. Its youthful naïveté added nothing to the laurels of the sophisticated writer he later became, and fortunately could not detract from them. And how could his kindly critic know that this awkward youth would one day sit beside him among "The Immortals" of the Académie Française?

In 1834, then, he commenced his studies in the medical school in Paris, developing a great skill in dissection, all the while considering that "anatomy is the basis for medical investigation but in itself, anatomy teaches nothing without observation of the living". He lived frugally, sometimes tutoring in a girls' school to eke out his slender resources. The glamour of the Quartier Latin is not so apparent to him who needs must live there. In 1836 he became an extern and in December 1839 passed a competitive examination for intern and

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thus came under the eye of Magendie, chief of a service at the Hôtel-Dieu, and Professor of Medicine in the Collège de France. The latter post was essentially a research position; the lectures he gave were intended for advanced students and there were some meagre laboratory facilities provided for demonstrations. In 1841, Bernard was officially made *préparateur* for Magendie. Without doubt, Magendie was the foremost physiologist in France at the time, and Bernard was overjoyed to receive this opportunity and incidentally a small salary alleviated his financial discomforts. Here he was to work the rest of his life, for some years during Magendie's illness deputizing for him. No paper jointly authored by Magendie and Bernard exists, though Magendie frequently gave him credit for assistance. The appointment, however, gave him the opportunity to initiate his own researches. It is interesting to note how many investigations were carried on, apparently simultaneously, and subsequently elaborated over the years as new facts were discovered.

The state of physiology in Bernard's early days was, to say the least, deplorable. While physics and chemistry were fast emerging from alchemy, the life processes were regarded as something unknowable. Vitalism was supposed to make a contribution which assured that physiology could never be unravelled. It negated the physical and chemical laws governing the inanimate. Science in France was nationalistic, and the dicta of the great dominated the picture. Nowhere was the influence of the great morphologist, Cuvier, more respected. Profoundly influenced by a vitalistic bias, disdainful of the growing application of newer methods, he believed that physiological investigation could produce only errors. Bichat, though he died at 31, still a vitalist, really struck a fatal blow to this doctrine when he distributed the functions of the body to its various organs and tissues and believed life to be a synthesis of these into harmony. It is unfortunate that Bichat did not live long enough to realize the implications of his later beliefs and his students and successors were not capable of expanding upon them but contented themselves with perpetuating the old errors. Magendie was the man-in-between. He was willing to believe (if it could be proved) that some things were inexplicable, but if the matter could be resolved by experiment, then he would and did do that experiment. This was what was needed at the time, and a more systematic approach would have taken him much further and probably eliminated some of his erroneous conclusions. Magendie was also an inborn sceptic. He doubted his own results even as he produced them. Within limits this is a valuable trait if profitably applied, but Magendie failed to do so. Such was the master whom Claude Bernard admired, though at the same time fully aware of his faults, and he owed much to him.

If the state of physiology was deplorable, that of clinical medicine was not less so. Having no physiology as a background, medicine could still observe, record and debate. But shrewd men there have been, and perhaps over the years they have given the physiologists as much as they have received and sometimes have remained humble about it. Claude Bernard may rightly be regarded as the father of modern medicine though he never practised. Father, not only in what he did, and that was much, but also in what he said. The principles he employed to elucidate a problem, he set forth in writing time and again but nowhere more beautifully than in his *Introduction to the Study of Experimental Medicine.* It was received with warm approval throughout the scientific world, not only for its clarity of exposition but indeed for its literary style. "You have created a new style," said M. Patin, as he welcomed him into the Académie Française in 1869. (After which Bernard delivered the Éloge to his predecessor, Flourens, a finished production, but rather cold and lacking in the charm and originality of the "Introduction".)

Bernard's first paper was published in 1843 and is of interest from an anatomical standpoint though having a physiological point as well. His well-known skill in dissection was employed in an attempt to discover an anastomosis between the pneumogastric and facial nerves. By chance, the sense of taste was found to be diminished on the operated side and the direction of the investigation was changed to involve the chorda tympani. With the "instinct of genius", as Foster has called it, he altered the whole course of the investigation to follow up a newly made observation, as he was to do so many times later on.

His thesis for the Doctorate in Medicine—1843—was the first of a long series on various aspects of digestion and nutrition. He showed that cane sugar was altered by gastric juice so that when injected into the blood it was no longer recoverable in the urine, whereas untreated cane sugar is excreted unchanged.

He was then free to commence his remarkable series of researches, and numerous papers rapidly appeared, some alone, but several jointly with a young chemist, Barreswill, and several others with Duvaine, Pelouze, Rayer, Brown-Sequard, Charcot and Robin. Four times he won the prize for experimental physiology of the Académie des Sciences. On the second occasion, the coveted red ribbon of the Legion of Honour was conferred upon him. He was not to receive the prize a fifth time, for in 1854 he was elected a member of the Academy and became chairman of its Jury of Award. Whether this was good politics cannot be said; certainly his greatest discoveries were yet to be described, though foreshadowed by numerous smaller communications to the Société de Biologie, of which he was a founder and vice-president and, after the death of Dr. Rayer, elected perpetual president.

While the earlier French physiologists were largely influenced by the beliefs of their forebears, and Bernard can be thought of as one of the first

to break away, the situation in other lands was no less disturbing. A sharper cleavage from vitalism perhaps, but the German masters whom we recall were contemporaneous with Bernard or followed after him. Some excellent physiological work was being done in Britain but Italy contributed little. In America, the most noteworthy work was Beaumont's observations on digestion in the stomach of the French Canadian, Alexis St-Martin.

While some French physiologists were doing a limited amount of good work, Magendie's pupil and successor grasped firmly the principle that experiments should be done to demonstrate the worth of an idea and not merely to see what would come of it, as Magendie did. In other words, he systematized his work: first an idea, then the design of the appropriate experiment to test it, then meticulous observation and recording of the result, and finally, meditation on its meaning and implications.

To Bernard, there were no unsuccessful experiments. He firmly believed that the results were always the true consequence of the conditions of the experiment; if the results were unexpected, he understood that the conditions were likewise modified by some unknown or unnoticed variation or circumstance and that this must be sought out. A proper experiment, if repeated, would always result in the same way.* Of course he realized that some things were not open to experiment with the methods available in his day and might perhaps never be known, but this was far removed from the old vitalism which, in effect, forbade all trial and at which he charged vigorously on every possible occasion. He championed the view that life processes obeyed the same physico-chemical laws as inanimate nature.

Bernard was married in 1845; two daughters lived after him but, to his intense grief, two sons did not survive their infancy. The marriage was a failure from the outset, with incompatibility and inconsiderateness not confined to either party. Formal separation, however, was postponed until 1870. The daughters, sympathizing with her views, left with their mother, though there is later evidence of affectionate relations with their father. Bernard, himself, said little, and that rarely, even to his closest friends, who watched with anxiety. Most of them had never known Mme. Bernard. Some considered her slightly mentally unbalanced but this is a borderland area and her behaviour was not without provocation. No one will know how much this marital disharmony did to drive Bernard to his laboratory and to outside interests, but his pattern of life was already well established before the marriage; his solace, a retreat to the hills of "smiling Beaujolais".

*Perhaps this was nowhere better illustrated than in his experiments on puncture of the medulla causing glycosuria. The first one gave unmistakably positive results. Then eight or 10 attempts failed, but why had the first one succeeded? In subsequent experiments he found that the area which must be injured is very small and that only on the first occasion had he actually damaged it.

Presumably he encountered the age-old fallacy that two can live as cheaply as one, since we find him undertaking outside work to supplement an insufficient income. He made the anatomical dissections for the atlas of anatomy published by Jacob and Bourgery, and published jointly with Ch. Huette an illustrated textbook of surgery which was very successful. Private lectures, demonstrations and tutoring were not a very satisfactory solution to his problem. Truth to tell, many have observed that he was not at this time a very competent lecturer, embarrassed, somewhat stumbling and awkward at the outset until he caught fire from the events of his demonstration. Indeed he lost the contest of the *Concours pour l'agrégation* to more fluent speakers, but in 1847 began to give the course of lectures as *suppléant* for Magendie and in 1855 he succeeded him as Professor of Medicine in the Collège de France. In the previous year, however, a new chair in general physiology was created in the Faculty of Sciences at the Sorbonne, and Bernard became its first occupant. There was no laboratory space coupled with this chair, and the cubbyhole at the Collège de France was too small for two investigators. Bernard was fortunate in his friends who supplied working places for many of his researches during the earlier years.

It is not intended to discuss all the investigations which Claude Bernard initiated. Today, many a scientific contribution or review must start with the words "In 18—, Claude Bernard showed. . . ." Nor is it easy to trace the sequence of events which contributed to the finished picture. Mostly these are to be found in small advances communicated to the Société Philomathique, the Société de Biologie, the Académie des Sciences, and very often in the "Leçons"—the notes of his lectures at the Collège de France or the Sorbonne taken by one of his students and revised by him. This was a procedure followed by Magendie before him and continued by Bernard, with some irregularities associated with illness, throughout his life. Bernard did not like to write—the earliest communication was usually a bald recital of facts telling nothing of the vision of the man; as additional facts were added the picture grew clearer, and in his later summaries the broad grasp of biological truths the man possessed became apparent and simple even to the uninitiated. But though he was at pains to trace back the idea to its early beginnings, there is apparent in his later writings a maturity founded on innumerable experiences, sometimes pleasant and often disappointing, accumulated over the years. He never became a philosopher, he never founded a system, he realized that his science was still too young for such a luxury. Largely, he avoided generalizations, though not always successfully. With a profound respect for mathematics, he regarded statistics with a suspicion not unjustified in his day. With recent advances, of course, the situation is much better, but its applicability to a given case may sometimes, perhaps often, be

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rightly questioned by statistician and biologist alike. The designing of the experiment to supply the answers, as Bernard insisted, is still all-important.

It would be incorrect to attribute to Bernard powers of divination. At some point, it is true, he could see further than at others, but he had the joy of success—of surmounting some intermediate steps to knowledge of the whole along the way, and ended with a broad grasp of the value of all the steps and many times an insight into its future importance. And thus he has illumined our further progress—yes, our *future* progress.

In his time the pancreas was known to digest starch. Bernard noticed that in rabbits fed only on meat the lacteals were filled with milky chyme but, differing from dogs, it appeared some 30 centimetres or more from the pylorus, corresponding thus to the entrance of the pancreatic secretion into the intestine. By adding crushed pancreatic tissue, he found that neutral fat was split into fatty acid and glycerin. Furthermore, starch is split into sugars. The same results were found with pancreatic secretion. With regard to proteins, he thought that the pancreas completes gastric digestion—only a part of the truth. But if starch is changed to glucose, if cane sugar is changed to a monosaccharide before absorption, what becomes of the sugar? A long train of investigations thus initiated led to the discovery of glycogen, properly regarded as one of Bernard's greatest achievements. That some associated conclusions were incorrect does not detract from the far-reaching importance to physiology of this discovery. His discovery of the vasomotor system was only accomplished over many years of patient experimentation. Its importance in the control of blood supply to the tissues can hardly be overemphasized either in experimental medicine or the day-to-day practice of clinical medicine. His work on curare and other poisons is largely concerned with their use as tools for the elucidation of problems in experimental medicine. But the later use of curare and its congeners for overcoming certain difficulties in modern medicine is based on the work of Bernard and other investigators. The brilliant exposition of the action of carbon monoxide, the location of oxygen transport in the pigment of the red blood cells antedated some of the remarkable spectroscopic researches of Hoppe-Seyler on hemoglobin and its derivatives by some years, though it is but just to regard them as complementary and contemporaneous. Certainly they were independent and Bernard accorded them full credit.

Up to the time of his transfer to the chair of general physiology at the Museum of Natural History (1870) these and many other investigations were undertaken by him to elucidate immediate medical problems and furnish a rational background for medical practice. A gradual change occurred. During his many years of active investigation he developed a broader viewpoint which included both plant and animal life. He had shown that not merely plants but animals as well could produce compounds, e.g. sugar and starch or glycogen, in refutation of the theory by Dumas, who held that plant life is constructive, animal life, destructive. He also showed that both plants and animals are affected by anesthetics and that they share other similarities. Particularly useful is his viewpoint that organs interdependently cooperate in bringing about a certain result and that a properly designed experiment would always bring about the same result. These are truisms today which do not require the emphasis Bernard then placed upon them. He was never concerned with ultimate causes; experimental medicine can only answer "how?" and never "why?" Since the time of Lavoisier, it had been commonly held that combustion took place in the lungs. Doubly armed with the skill of DeArsonval, his pupil and successor at the Collège de France, with electrical instruments Bernard showed that the combustion actually occurred in the tissues, the basis of our modern views of tissue respiration.

In earlier days the isolation of glycogen, the discovery of vasomotor nerves, the functions of the pancreas, the site of production of animal heat, and many another investigation of lesser importance, done meticulously in accordance with a predetermined idea and method of investigation, were regarded as the most important elements establishing his greatness. With a wealth of experience behind him, much greater than any of his predecessors, and an innate ability, a characteristic of the man, he launched one of his few generalizations, more prophetic possibly than he realized at the time, a concept which has borne much fruit and perhaps has dominated experimental medicine and practical medicine alike in the last half century. No prophetic hypothesis this, springing like Athena full-armed from the head of Zeus, but creeping from small beginnings and gaining new rootlets from every joint as it grew, it became to him a certainty and today may be the most important idea in general physiology, including pathology, psychology and the other life sciences. Briefly stated, without the myriad modifications of varying circumstances, the concept of *le milieu intérieur*, the blood and tissue fluids, consists in the existence of a sort of inner environment, isolated, insulated from the external environment which permits and controls and regulates the disparate functions of cells, which, acting independently and interdependently, release it from external controls. But it was verging on prophesy when he stated, "We shall be able by modification of the internal environment, the blood, to exercise our will on all this world of elementary organisms composing our body when we know the laws which control their diverse relationships, we shall be able to regulate and modify to our taste vital manifestations." But how very much of this has come true! And when we admit that the internal environment provides a medium in which the sheltered cell may act and

react upon itself and respond to the activities of other cells, then we approach molecular biology of modern days and perhaps the last great challenge to vitalism, of which Claude Bernard was always so vigorous an opponent.

It is interesting to note how he impelled the friendship and admiration, even the veneration, of the sons of his friends. Doubtless this had a relationship to the early loss of his own sons. As his reputation grew, he attracted from France itself, and from other countries, students of quality: Burdon-Sanderson, later of Oxford, and Pavy, Wier Mitchell and Dalton, Sechinev, the father of Russian physiology and teacher of Pavlov; Willy Kühne and many another, by the charm of his manner, the dexterity of his hands, the clearness of his intellect and his moral worth, for indeed he worshipped truth. But his friendship extended further among the admirable in many disciplines: art, music, philosophy, even politics, as well as various branches of science—a many-sided man gifted to appreciate the best wherever found. To him came honours and rewards; to name them all could be tiresome, to omit some would seem invidious. The best work of his life was accomplished in the score of years following his doctorate in medicine. Though later sometimes ill for long periods, he was not inactive; he continuously polished his science until the last days, but left much still incomplete, being overburdened by ephemeral responsibilities thrust upon him.

As a political animal Bernard was first of all a Frenchman, from his choice of friends probably an Orleanist, as indeed the repressive policies of Charles X would seem to have directed a considerable majority of the people. In later days an Imperial decree of Napoleon III made him a Senator for life. But 1870 changed all that, and he favoured the republican element mainly because of the vigorous activity they displayed in ridding the country of the German occupation. He had friends in all parties, however, throughout his life and, apart from being a Frenchman loyal to the existing régime, he had a tolerance unusual in his time.

Throughout his later years he was much troubled by sciatica and by respiratory infections, but nevertheless struggled to complete his lecture courses and continue his laboratory investigations. According to Paul Bert, on the last day of the year symptoms arose which heralded a severe illness which proceeded rapidly and he succumbed on February 10, 1878. Six days later, with impressive ceremonies formerly associated only with Royalty, the Marshals of France and great political figures, he was laid to rest in Père Lachaise with his infant sons. The determinant cause appears to have been an acute pyelonephritis but there are reasons for supposing this to be a fulminant end to long-standing disease, and which today, as a result of the stimulus to medical science he initiated, could have been delayed, if not aborted, by appropriate treatment.

Regretfully one must speak of another matter. During his last vacation at Saint-Julien, Bernard occupied himself with some investigations on fermentation. His great friend of many years, Pasteur, whom he had so many times assisted, being without a biological insight, could not explain his results without falling back on vitalism. Many years before, Bernard had warned of the inadequacy of such an explanation. After the death of Bernard, these brief notes, these memoranda to himself to clarify his thinking and hidden carefully away at Saint-Julien, were found and published. Bernard, himself, in his last days considered them incomplete, as indeed they were. Pasteur was astonished and reacted violently in reply, futilely however, as he really begged the question. Much controversy followed, but many years later Buchner isolated the enzyme from the yeast cell which Bernard was apparently seeking, and accomplished the fermentation. Thus the matter ended. Pasteur was correct about his facts, wrong as to the interpretation. He lacked the broader appreciation of biology which Bernard possessed and the ability to avoid premature and incomplete publication of results, but not less than did Bernard's successors.

Many scientists we account great in their day and generation and this is proper. A notable few come at the proper time in history, have or make opportunity for their genius to flower, develop irrefutable advances and affect the future of science for generations to come. Of such was Claude Bernard. Said his friend and admirer, Gambella, speaking in the Chamber of Deputies, "The light, which has just been extinguished, cannot be replaced."

For those interested further, there are two biographies in English, Sir Michael Foster's "Claude Bernard", published in 1899, and Professor J. M. D. Olmsted's "Claude Bernard, Physiologist". For both I wish to express my appreciation. From both I have borrowed much. Foster's book is lucid, can be read in an evening or two, contains the essential facts (with but few errors) and shows Bernard's work through the eyes of a master half a century later in time, during which a glorious springtime in medical science had blossomed all over the Western World. It is a competent piece of journalism, but his Claude Bernard never offered a friend to taste of his own home-produced Beaujolais, and most surely he was never "très gai". Now what shall one say of the labours of Olmsted, a longtime friend, sometime Professor of Physiology of the University of Toronto? It is undoubtedly a labour of love, sprinkled with the inconsequential details that illustrate so much of character and wisdom and adorned with sidelights emanating from others, contemporary with Bernard, which place him in his proper atmosphere. It is properly critical, in a scientific sense, of his accomplishments and of his errors in a way that only a biological scientist familiar with modern physiology and adequately trained could be. But you do feel that his man really lived. Having owned a copy of "Claude Bernard" since 1910, I was grateful for Olmsted's reinterpretation in 1937. Now, some 25 years later, a new interpretation in the light of more recent physiological investigations would be useful. For experimental medicine has not stood still in these later days.

The other indispensable text is the translation by H. C. Greene of Bernard's "Introduction to the Study of Experimental Medicine", but one should read, first of all, Lawrence Henderson's sensitive introduction to the translation and the appreciation by his favourite pupil and successor at the Sorbonne, Paul Bert, written two days after the death of the master.